UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

AZURITY PHARMACEUTICALS, INC., Plaintiff, v. BIONPHARMA INC., Defendant	)	Civil Action No. 21-12870 (MAS) (DEA) [redacted] **Public Version**

DEFENDANT BIONPHARMA'S OPPOSITION TO PLAINTIFF AZURITY'S MOTION FOR ORDER TO SHOW CAUSE WITH TEMPORARY RESTRAINTS, PRELIMINARY INJUNCTION, AND OTHER EMERGENT RELIEF

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TABLE OF ABBREVIATIONS

Abbreviation	Meaning
'008 patent	U.S. Patent No. 9,669,008 B1 (ECF No. 9-3, 7/13/21 Shrestha Decl. Ex. C)
'023 patent or patent-in-suit	U.S. Patent No. 11,040,023 B2 (ECF No. 1-1, Compl. Ex. A)
'442 patent	U.S. Patent No. 9,808,442 B2 (ECF No. 9-4), 7/13/21 Shrestha Decl. Ex. D)
'482 patent	U.S. Patent No. 10,786,482 B2 (ECF No. 9-12, 7/13/21 Shrestha Decl. Ex. L)
'587 application	U.S. Patent Application No. 17/150,587, the prosecution history of which is attached as Ex. V to the 7/13/21 Shrestha Declaration (ECF No. 9-22)
'587 PH	Prosecution history of the '587 application, attached as Ex. V to the 7/13/21 Shrestha Declaration (ECF No. 9-22)
'621 patent	U.S. Patent No. 10,918,621 B2 (ECF No. 9-13, 7/13/21 Shrestha Decl. Ex. M)
'745 patent	U.S. Patent No. 10,039,745 B2 (ECF No. 9-5, 7/13/21 Shrestha Decl. Ex. E)
'747 patent	U.S. Patent No. 8,568,747 B1 (Ex. Q to the Moreton Declaration submitted concurrently herewith)
'868 patent	U.S. Patent No. 10,772,868 B2 (ECF No. 9-11, 7/13/21 Shrestha Decl. Ex. K)
'987 patent	U.S. Patent No. 10,154,987 B2 (ECF No. 9-6, 7/13/21 Shrestha Decl. Ex. F)
Amneal	Amneal Pharmaceuticals LLC
ANDA	Abbreviated New Drug Application pursuant to 21 U.S.C. § 355(j)
Asserted Claims	Claims 1-6, 10, 12-16, and 19 of the '023 patent, which Azurity asserts in connection with its Motion
Azurity	Plaintiff Azurity Pharmaceuticals, Inc., successor-in-interest to Silvergate Pharmaceuticals, Inc.

Abbreviation	Meaning
Azurity's enalapril liquid patent family	'008, '442, '745, '987, '482, '868, '621, and '023 patents
Azurity's Motion	ECF No. 24, Plaintiff Azurity's Motion for Order to Show Cause for Temporary Restraining Order, Preliminary Injunction, and Other Emergent Relief
Azurity's Brief or Azurity's OTSC Brief	ECF No. 25, Brief in Support of Plaintiff Azurity's Order to Show Cause for Temporary Restraining Order, Preliminary Injunction, and Other Emergent Relief
Bionpharma	Defendant Bionpharma Inc.
Bionpharma's ANDA	Bionpharma's ANDA No. 212408
Bionpharma's ANDA product	The 1 mg/mL enalapril maleate oral solution described in Bionpharma's ANDA
Bionpharma's Motion to Dismiss	ECF No. 8, Defendant Bionpharma's Motion to Dismiss Pursuant to Fed. R. Civ. P. 12(b)(6)
Bionpharma's MTD Brief	ECF No. 8-1, Defendant Bionpharma's Brief in Support of its Motion to Dismiss Pursuant to Fed. R. Civ. P. 12(b)(6)
Bionpharma's Motion to Transfer	ECF No. 7, Defendant Bionpharma's Motion to Transfer Venue Pursuant to 28 U.S.C. § 1404(a)
Bionpharma's MTT Brief	ECF No.7-1, Defendant Bionpharma's Brief in Support of tis Motion to Transfer Venue Pursuant to 28 U.S.C. § 1404(a)
Dr. Buckton	Dr. Graham Buckton, Azurity's formulation expert in the instant suit
Buckton Declaration	ECF No. 25-6, Declaration of Dr. Graham Buckton
3/31/21 Byrn Declaration	D. Del. 18-1862 ECF No. 235, Mar. 31, 2021 Declaration of Stephen R. Byrn, Ph.D. in Supp. of Silvergate's Motion for Preliminary Injunction (attached as Exhibit B to the Moreton Declaration submitted concurrently herewith)
The common specification	The common specification of Azurity's enalapril liquid patent family
Devine Declaration	ECF No. 25-1, Declaration of Wendy L. Devine
D. Del. 18-1962	*Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A.

Abbreviation	Meaning
	No. 18-1962 (D. Del.) (the first of the First Wave Suits)
D. Del. 19-1067	*Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 19-1067 (D. Del.) (the second of the First Wave Suits)
D. Del. 20-1256	*Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 20-1256 (D. Del.) (the Second Wave Suit)
DOE	Doctrine of equivalence
Dr. Byrn	Dr. Stephen R. Byrn, Azurity's formulation expert in the First and Second Wave Suits
Dr. Chris Moreton or Dr. Moreton	Dr. R. Christian Moreton, Bionpharma's formulation expert
Epaned® Kit or the Kit	Azurity's predecessor product to Epaned® (ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 7), the prescribing information for which is attached as Ex. E to the Shrestha Declaration, submitted currently herewith
Epaned® Kit PI	Epaned® Kit Prescribing Information (Sept. 2014), attached as Ex. E to the Shrestha Decl. submitted concurrently herewith
FDA	United States Food and Drug Administration
FDA Stability Guidance	U.S. Food and Drug Administration, *Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products* (Nov. 2003, Rev. 2) (Ex. P to the Moreton Declaration, submitted concurrently herewith)
First Wave Patents	'008, '442, '745, and '987 patents
First Wave Suits	*Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. Nos. 18-1962 and 19-1067 (D. Del.)
JSD	Joint Stipulation for Dismissal entered in the Second Wave Suit (ECF No. 106), so ordered by the Court with a docket entry on May 21, 2021 (ECF No. 9-15, 7/13/21 Shrestha Decl. Ex. O)
Mr. McSorley	Mr. Robert McSorley, Bionpharma's irreparable harm expert
Moreton Declaration	Declaration of R. Christian Moreton, Ph.D., submitted concurrently herewith

Abbreviation	Meaning
4/19/21 Moreton Declaration	D. Del. 18-1962 ECF No. 247, April 19, 2021 Declaration of R. Christian Moreton, Ph.D. (attached as Ex. C to the Moreton Declaration, submitted concurrently herewith)
Mosher Decl.	Decl. of Gerold L. Mosher dated Apr. 23, 2021 (ECF No. 9-22, 7/13/21 Shrestha Decl. Ex. V, '587 PH at BION-ESOL00038480-88)
NDA	New Drug Application pursuant to 21 U.S.C. § 355(b)(1)
Orange Book	FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations*
Paragraph IV certification	Certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV)
PI	Preliminary injunction
POSA	Person of ordinary skill in the art
PTO or Patent Office	United States Patent and Trademark Office
Second Wave Patents	'868, '482, and '621 patents
Second Wave Suit	*Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 20-1256 (D. Del.)
Shrestha Decl.	The August 27, 2021 Declaration of Roshan P. Shrestha, Ph.D., submitted concurrently herewith
7/13/21 Shrestha Decl.	ECF No. 9, July 13, 2021 Declaration of Roshan P. Shrestha, Ph.D.
Silvergate	Silvergate Pharmaceuticals, Inc., predecessor-in-interest to Azurity
Third Wave Suit	The instant action, *Azurity Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 21-12870 (D.N.J.)
Wands Factors	Factors to evaluate undue experimentation in connection with non-enablement inquiry enunciated in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988): (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability in the art; and (8) the breadth of the claims

Abbreviation	Meaning
WD	Written description under 35 U.S.C. § 112(a)

Defendant Bionpharma respectfully submits the instant Opposition to Plaintiff Azurity's Motion for an Order to Show Cause for Temporary Restraining Order, Preliminary Injunction, and Other Emergent Relief (ECF No. 24) ("Azurity's Motion"). For the following reasons, Bionpharma respectfully requests that Azurity's Motion be denied.

INTRODUCTION

As explained in connection with Bionpharma's pending motions to transfer (ECF No. 7) and dismiss (ECF No. 8), this action represents the third wave in a series of lawsuits filed by Plaintiff Azurity against Bionpharma asserting that Bionpharma's ANDA No. 212408 ("Bionpharma's ANDA")—which describes a 1 mg/ml enalapril maleate oral solution as generic to Azurity's Epaned® antihypertensive prescription drug product ("Bionpharma's ANDA product") and was approved by FDA—and ANDA product infringe Azurity's enalapril oral liquid patent family. The First[1] and Second Wave[2] Suits were filed in Delaware Federal court, where the parties have spent over two and a half years litigating seven patents that are in the same family as the '023 patent that is the subject of the instant Third Wave Suit. Chief Judge Stark from the District of Delaware held a 5-day bench trial in the First Wave Suits on February 1-5, 2021. On April 27, 2021, Judge Stark issued a 72-page opinion finding that Azurity failed to prove infringement of the asserted claims of the First Wave Patents and, on April 29, 2021, entered final judgment in Bionpharma's favor. Judge Stark's decision in the First Wave Suits rendered moot Azurity's Second Wave Suit on collateral estoppel grounds, and the Second Wave Suit was dismissed on May 21, 2021 with prejudice, unless Azurity secures a decision on appeal of the First Wave Suits that eliminates the estoppel.

[1] *Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. Nos. 18-1962 and 19-1067 (D. Del.).

[2] *Silvergate Pharmaceuticals, Inc. v. Bionpharma Inc.*, C.A. No. 20-1256 (D. Del.).

In an effort to get away from Judge Stark and His Honor's findings and rulings in connection with the First and Second Wave Suits, including His Honor's finding that Azurity's expert in those suits lacked credibility, Azurity has filed the instant Third Wave Suit here in New Jersey, where Azurity seeks to assert the same cause of action that was litigated by the parties in connection with the First and Second Wave Suits, and that went to final disposition in Bionpharma's favor, by asserting a continuation patent—the '023 patent—with claims that are patentably indistinct from the claims of the First and Second Wave Patents.

Rather than respond in a timely fashion to Bionpharma's pending motions to transfer and dismiss, Azurity instead sought and secured extensions for its responses to those motions, all the while knowing that Bionpharma's ANDA was not subject to any 30-month stay of FDA approval, and that FDA could approve Bionpharma's ANDA any day, leading to an unrestricted launch by Bionpharma of its ANDA product. That possibility became reality: on August 10, 2021, FDA granted final approval of Bionpharma's ANDA, and Bionpharma launched its ANDA product a week later on August 17, 2021. Despite having actual knowledge on August 10, 2021 (or shortly thereafter) that Bionpharma's ANDA had received final approval, because FDA had publicly disclosed the approval,[3] ***Azurity waited nine more days to file the instant Motion seeking emergent relief***. Azurity should have filed any motion for emergent relief when it filed the instant Third Wave Suit (on June 22, 2021), and its attempt to blame Bionpharma for not producing FDA correspondence solely related to the timing of approval of Bionpharma's ANDA—which has nothing to do with the actual infringement, invalidity, and claim preclusion claims and defenses in this case and was therefore not discoverable under Rule 26(b)[4]—is simply a futile attempt to

[3] FDA posted its approval for Bionpharma's ANDA on August 10, 2021, or shortly thereafter, publicly on its website. ECF No. 25, Azurity's Br. at 6.
[4] *See* ECF No.34, 8/25/21 Bionpharma Ltr. to M.J. Arpert at 3 n.5.

deflect blame for a situation that was of Azurity's own making.

On the merits, Azurity's Motion must be denied, because Azurity cannot establish a likelihood of success with respect to at least the following defenses Bionpharma has raised:

Claim Preclusion: As explained in Bionpharma's Brief in support of its Motion to Dismiss (ECF No. 8-1), the claims of the '023 patent are patentably indistinct from the claims of the First and Second Wave Patents that Bionpharma previously defeated in Delaware, which means that Azurity is asserting the same cause of action in the instant suit that Bionpharma prevailed on in connection with the First and Second Wave Suits. Azurity devotes less than a page in its Brief (ECF No. 25 at 17-18) to discussing this defense, and applies an incorrect standard to argue that because the claims of the '023 patent are of broader scope than the claims of the First Wave Patents, claim preclusion does not apply. Azurity's arguments against claim preclusion are contrary to Federal Circuit precedent, and therefore Azurity cannot establish a likelihood of success on this defense.

Lack of Written Description: Azurity's First Wave Patents cover a very narrow group of enalapril liquid formulations—buffered with citric acid and sodium citrate at specific concentrations, and preserved with sodium benzoate at specific concentrations—that Azurity was able to establish were stable for 12 months under refrigerated conditions, a result that Azurity described as "unexpected" and that one of its experts argued defied conventional wisdom regarding enalapril liquids. Shortly after Bionpharma filed its ANDA, Azurity began filing patent applications seeking broader and different claim coverage (in an attempt to cover Bionpharma's ANDA product), including the application that eventually issued into the '023 patent. In contrast to Azurity's First Wave Patents, the claims of the '023 patent are of larger breadth, covering tens (and likely hundreds) of thousands of enalapril liquids that are never described in the common specification as being stable at refrigerated conditions for 12 months. ***What Azurity has claimed in the '023 patent is simply not what it actually invented***; no POSA would believe that Azurity had in its possession at the time it filed for the '023 patent tens (possibly hundreds) of thousands of enalapril liquids that are stable for at least 12 months, and the '023 patent claims are therefore invalid for lack of written description.

Non-Enablement: As both Azurity and its expert in the First and Second Wave Suits admitted, the POSA would believe that numerous liquids falling within the scope of the '023 patent claims are likely inoperable (i.e., they do not meet the stability requirements of the claims), and, as Bionpharma's expert (Dr. Chris Moreton) explains, the amount of experimentation it would take for a POSA to practice the full scope of the claims to determine which liquids were operable would not only be undue, it would be scientifically inconceivable.

Obviousness: If somehow this Court finds the '023 patent claims adequately supported, then Bionpharma respectfully submits that claims 1-6, 10, 12-16, and 19 ("Asserted Claims"), which each include within their scope enalapril liquids where the only preservative is a paraben or mixture of parabens, are obvious, as they essentially read-on Azurity's prior art Epaned® Kit.

Finally, Azurity cannot establish irreparable harm because it unduly delayed in filing the '023 patent, because it unduly delayed in seeking emergent relief in this action, and because, as explained below and in the accompanying declaration from Mr. Robert McSorley, Bionpharma's irreparable harm expert, damages from an at-risk launch would be easily quantifiable. The balance of hardships and public policy favor denial of Azurity's Motion, as Bionpharma waited patiently for over 32 months to launch its ANDA product, and prevailed over Azurity in three prior actions involving the same family of patents. The public interest favors the arrival of Bionpharma's lower-priced alternative to Azurity's Epaned®. Therefore, Azurity's Motion should be denied.

FACTUAL BACKGROUND

I. THE FIRST WAVE SUITS

Bionpharma filed its ANDA back in 2018, seeking approval from the FDA to market its ANDA product as generic to Azurity's Epaned®. ECF No. 1, Compl. ¶ 14. In response, Azurity instituted the First Wave Suits starting in December of 2018 in Delaware Federal court, asserting that Bionpharma's ANDA and the product described therein infringe Azurity's '008, ' 442, '745, and '987 patents ("First Wave Patents"). *Id*. at ¶¶ 14-15. The claims of Azurity's First Wave Patents are directed to: (1) a group of enalapril liquid formulations that contain citric acid and sodium citrate as a buffer system at specific concentrations, sodium benzoate as a preservative at specific concentrations, and that are stable for 12 months at refrigerated conditions (5±3 °C); and (2) methods of treatment using those liquids. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 5-19; ECF Nos. 9-3 - 9-6, 7/13/21 Shrestha Decl. Exs. C-F, First Wave Patents at claims. Bionpharma had designed its ANDA product extensively around Azurity's First Wave Patents, including by entirely omitting a buffer from its formulation, and by utilizing an alternative to the claimed sodium benzoate preservative. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 2.

The Delaware court held a five day bench trial on February 1-5, 2021 and, on April 27,

2021, issued its Opinion finding the asserted claims of Azurity's First Wave Patents not infringed by Bionpharma's ANDA product, including because Azurity failed to prove the existence of a buffer in Bionpharma's ANDA product, and because the alternative to the claimed sodium benzoate that Bionpharma used in its ANDA product was disclosed in the common specification of the First Wave Patents, but not claimed, and was therefore dedicated to the public. *Id*. at *1. The Court entered final judgement in Bionpharma's favor shortly thereafter. ECF No. 9-8, 7/13/21 Shrestha Decl. Ex. H, D. Del. 18-1962 ECF No. 270, Final J.; ECF No. 1, Compl. ¶ 14 n.2.

II. THE SECOND WAVE SUIT

Shortly after Bionpharma filed its ANDA, Azurity began filing continuation patent applications seeking considerably broader and different claim coverage, and eventually secured issuance of the '868, '482, and '621 patents ("Second Wave Patents") in late 2020 and early 2021, which were the subject of Azurity's Second Wave Suit. ECF No. 1, Compl. ¶ 16 n.4; ECF No. 9-10, 7/13/21 Shrestha Decl. Ex. J, Second Wave Suit ECF No. 49, Second Am. Compl.; *id*. at Exs. K-M (ECF Nos. 9-11 - 9-13), Second Wave Patents at covers. As explained above, on April 27, 2021, the Delaware court issued its opinion in the First Wave Suits finding that, *inter alia*, Azurity failed to prove the existence of a buffer in Bionpharma's ANDA product. Because all of the claims of the Second Wave Patents require a buffer (ECF Nos. 9-11 - 9-13, 7/13/21 Shrestha Decl. Exs. K-M, Second Wave Patents at claims), the Delaware court's finding that Azurity failed to prove the existence of a buffer rendered moot Azurity's Second Wave Suit on collateral estoppel grounds, and the parties stipulated to dismissal of the Second Wave Suit, which was so ordered on May 21, 2021. ECF No. 9-15, 7/13/21 Shrestha Decl. Ex. O, Second Wave Suit ECF No. 106, JSD; Second Wave Suit, May 21, 2021 docket entry. By the express terms of the dismissal order, all claims of the Second Wave Suits were dismissed with prejudice, except in the event "that the

Federal Circuit renders a decision whereby collateral estoppel would not apply to bar [Azurity's] assertion of the Second Wave Patents against Bionpharma." ECF No. 9-15, 7/13/21 Shrestha Decl. Ex. O, Second Wave Suit ECF No. 106, JSD at 3.

III. THE INSTANT THIRD WAVE SUIT

A. The '023 Patent

On January 15, 2021, over two years after Bionpharma filed its ANDA with the FDA and the institution of the First Wave Suits, Azurity filed with the PTO U.S. Patent Application No. 17/150,587, which claims priority to the First and Second Wave Patents. ECF No. 1-1, Compl. Ex. A, '023 patent at cover. On June 22, 2021, the '587 application issued into the '023 patent, and Azurity instituted this Third Wave Suit that same day. ECF No. 1, Compl. The claims of the '023 patent are very similar to the claims of the First and Second Wave Patents, and are directed to enalapril liquid formulations that may contain, but that do not explicitly require, a buffer component, and that are stable for at least 12 months at refrigerated conditions. ECF No. 1-1, Compl. Ex. A, '023 patent at claims.

B. Prosecution History of the '023 Patent

Bionpharma has provided a summary of the relevant portions of the prosecution history of the '023 patent at pages 5-6 of its MTD Brief (ECF No. 8-1), and the Court's attention is respectfully directed to those pages for that summary.

C. Approval and Launch of Bionpharma's ANDA Product

With the institution of the First Wave Suits, Bionpharma's ANDA had been subject to a 30-month injunctive stay that expired on April 30, 2021. ECF No. 25-2, Devine Decl. Ex. 9. On August 10, 2021, the FDA granted final approval of Bionpharma's ANDA. Shrestha Decl. Ex. A, 8/10/21 Approval Ltr. Bionpharma launched its ANDA product on August 17, 2021, and the instant Motion followed.

ARGUMENT

I. LEGAL STANDARD

"In determining whether to issue a preliminary injunction, the Court should consider the following four factors: "'(1) the likelihood of the patentee's success on the merits; (2) irreparable harm if the injunction is not granted; (3) the balance of hardships between the parties; and (4) the public interest.'" *AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579, 587 (D.N.J. 2009) (quoting *Abbott Labs. v. Andrx Pharms., Inc.*, 473 F.3d 1196, 1200-01 (Fed. Cir. 2007)). "[C]ase law and logic both require that a movant cannot be granted a preliminary injunction unless it establishes *both* of the first two factors, *i.e.*, likelihood of success on the merits and irreparable harm." *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001). "If [Bionpharma] raises a substantial question concerning either infringement or validity, *i.e.*, asserts an infringement or invalidity defense that the patentee cannot prove 'lacks substantial merit,' the preliminary injunction should not issue." *Id*. at 1350-51. The standard for a TRO is the same. *Interior Motives, Inc. v. Salvatore*, Civ. No. 20-5178, 2020 WL 2611517, at *2 (D.N.J. May 22, 2020).

II. AZURITY CANNOT ESTABLISH A LIKELIHOOD OF SUCCESS

As explained below, Azurity is precluded from asserting the '023 patent against Bionpharma, and the Asserted Claims are invalid.

A. Claim Preclusion Bars the Instant Third Wave Suit

Bionpharma has a motion to dismiss raising this legal defense currently pending before this Court. ECF No. 8. Azurity has repeatedly delayed responding to Bionpharma's Motion to Dismiss, and devotes less than a page in its Brief (ECF No. 25) to discuss this defense. That brief discussion, though, illuminates the strength of Bionpharma's claim preclusion defense, and why Azurity cannot establish a likelihood of success on this defense: Azurity completely fails to explain

how the claims of the '023 patent are patentably distinct from the claims of the First and Second Wave Patents that Bionpharma previously defeated.

In fact, it appears that one strategy Azurity is trying to employ to rebut Bionpharma's claim preclusion defense is to obscure the Federal Circuit's holding in *SimpleAir Inc. v. Google LLC*, 884 F.3d 1160 (Fed. Cir. 2018). In its Brief, Azurity provides the following quote from *SimpleAir*—"[W]here different patents are asserted in a first and second suit, a judgment in the first suit will trigger claim preclusion only if the scope of the asserted patent claims in the two suits is essentially the same" (ECF No. 25, Azurity's Br. at 17 (quoting *SimpleAir*, 884 F.3d at 1167)—to apparently argue that a change in claim scope by omitting a limitation contained in the claims of a first patent necessarily eliminates a claim preclusion defense to a second patent with claims that omit the limitation. That is, Azurity appears to be arguing that if the claims of a continuation patent are broader in scope than the claims of a parent patent, claim preclusion cannot apply. This is legally incorrect and stems from Azurity's selective quotation of the holding in *SimpleAir*—Azurity neglects to mention in its Brief that the Federal Circuit in *SimpleAir* went on to hold in the very next sentence that "***claims which are patentably indistinct are essentially the same***." *SimpleAir*, 884 F.3d at 1167 (emphasis added). As explained in Bionpharma's Motion to Dismiss Brief (ECF No. 8-1 at 10), well settled Federal Circuit law holds that "[a] later patent claim 'is not patentably distinct from an earlier claim if the later claim is obvious over, or anticipated by, the earlier claim.'" *In re Hubbell*, 709 F.3d 1140, 1145 (Fed. Cir. 2013) (quoting *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001)).

As also explained in detail in Bionpharma's Motion to Dismiss Brief—which Azurity has had in its possession for now almost 6 weeks—nearly all of the claims of the '023 patent are anticipated by the claims of the First and Second Wave Patents, and the few that are not are clearly

obvious over those claims. ECF No. 8-1, Bionpharma's MTD Br. at 12-21. In further support of those claim preclusion arguments, Bionpharma submits concurrently herewith a declaration from its pharmaceutical formulation expert, Dr. Chris Moreton, who explains in detail how each claim of the '023 patent is anticipated or rendered obvious by the claims of the First and Second Wave Patents. Moreton Decl. ¶¶ 42-64. Despite having had Bionpharma's Motion to Dismiss Brief and the "patentably indistinct" arguments contained therein for almost 6 weeks, Azurity fails to even address those arguments in its Motion Brief. *See* ECF No. 25, Azurity's Br. at 17-18. Azurity does not refute, ***let alone address***, Bionpharma's contention that the claims of the '023 patent are anticipated, or rendered obvious, by the claims of the First and Second Wave Patents, and are therefore patentably indistinct from those claims. Bionpharma respectfully submits that Azurity has waived any such arguments, and cannot establish a reasonable likelihood of success on this defense.

The only other argument against claim preclusion that Azurity musters in its brief is that the preservative limitations of the '023 patent claims are "meaningfully different" because they include parabens or mixtures of parabens, whereas, "[i]n the prior case, the claims of the asserted patents all literally required a formulation that contained sodium benzoate." ECF No. 25, Azurity's Br. at 18. But Azurity overlooks that several claims of the Second Wave Patents—including all of the claims of the '621 patent—recite enalapril liquids where the preservative is a paraben or mixture of parabens. *See, e.g.*, ECF No. 8-1, Bionpharma's MTD Br. at 19-21; ECF No. 9-13, 7/13/21 Shrestha Decl. Ex. M, '621 patent at claims. Moreover, the argument is misplaced and incorrect—it matters not that the preservative limitation of certain claims of the '023 patent recite "sodium benzoate, a paraben, or mixture of parabens," as opposed to just sodium benzoate. ECF No. 25, Azurity's Br. at 18 (citing ECF No. 1-1, Compl. Ex. A, '023 patent at claim 1). What

matters for claim preclusion purposes is whether the claims of the '023 patent are ***patentably indistinct*** from the claims of the First and Second Wave Patents. As Bionpharma has demonstrated in its Motion to Dismiss Brief (ECF No. 8-1 at 12-21), and as Dr. Moreton persuasively explains at paragraphs 42-64 of his Declaration, they are, and Azurity is therefore asserting the same cause of action that the parties litigated in the First and Second Wave Suits. Claim preclusion therefore bars this suit, and Azurity cannot establish a likelihood of success on this defense.

B. The '023 Patent Claims Are Invalid

What Azurity has claimed in '023 patent is not what it invented. Because of this, as explained below and in the accompanying Moreton Declaration, the '023 patent claims are invalid for lack of written description ("WD") and non-enablement. If, somehow, the Court finds the '023 patent claims adequately supported, then at least the Asserted Claims are invalid as they essentially cover an obvious version of the Azurity's prior art Epaned® Kit.

1. The '023 Patent Claims Lack Adequate Written Description

35 U.S.C. § 112(a) requires, *inter alia*, that a patent specification contain a WD of the claimed invention that "clearly allows [a POSA] to recognize that the inventor invented what is claimed." *Ariad Pharm., Inc. v. Eli Lilly & Co*., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (internal quotations and brackets omitted). "[A] description which renders obvious a claimed invention is not sufficient to satisfy the [WD] requirement." *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1567 (Fed. Cir. 1997). The WD of the claimed invention must be sufficient to "reasonably convey[] to [a POSA] that the inventor had possession of the claimed subject matter ***as of the filing date***." *Id*. (emphasis added). This "requires an objective inquiry into the four corners of the specification from the perspective of [a POSA]," *id*., and "an affidavit or declaration [submitted] during prosecution . . . does not cure [a] lack of [WD] in the specification, [which is] required by statute," *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 969 (Fed. Cir. 2002).

Importantly, when a patent claims a genus using functional language to define a desired result—as is the case with the '023 patent claims, with each requiring stability under refrigerated conditions for at least 12 months—"the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus." *Ariad*, 598 F.3d at 1349. To comply with the WD requirement, functionally-defined genus claims must be supported by "a reasonable structure-function correlation . . . whether by the inventor as described in the specification or known in the art at the time of the filing date." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014). "[W]hen the inventor expressly claims [a] result, [Federal Circuit] case law provides that ***the result must be supported by adequate disclosure in the specification***." *Nuvo Pharm. (Ir.) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1368, 1384 (Fed. Cir. 2019) (emphasis added). A claim may not "merely recite a description of the problem to be solved while claiming all solutions to it and, . . . , cover any [formulation] later actually invented and determined to fall within the claim's functional boundaries." *Ariad*, 598 F.3d at 1353. That is exactly what Azurity has done here with the '023 patent.

a. Enalapril: Unstable and Unpredictable

As Azurity and its expert in the First and Second Wave Suits, Dr. Byrn, have admitted, the POSA would know that enalapril is inherently unstable in liquid formulations and whether any given enalapril liquid is capable of being stable for at least 12 months or longer is entirely unpredictable. ECF No. 25-2, Devine Decl. Ex. 3, D. Del. 18-1962 ECF No. 193, Trial Tr. Vol. A, 52:25-53:7 (Azurity's Opening Statement: "Another problem Amneal has is the unpredictability in the art. . . . [C]ould a [POSA] predict the ingredients needed to achieve a liquid form of enalapril . . . that would be stable for the required 24-month shelf life? The answer is

no."). In a declaration, Dr. Byrn, explained that enalapril "is known to have stability issues once dissolved into a solution," and that "a liquid formulation of enalapril would generally be expected to have a short shelf-life (e.g., on the order of weeks to only a few months)." Moreton Decl. ¶ 84; *id*. at Ex. G, D. Del. 18-1962 ECF No. 235, 3/31/21 Byrn Decl. ¶ 15.

As the Delaware court found at trial, during prosecution of the First Wave Patents, Azurity narrowed its application claims to correspond to the Example E liquids disclosed in the common specification (ECF No. 1-1, Compl. Ex. A, '023 patent 36:43-37:40)—which, as explained below, are the only enalapril liquids described in the specification as being stable for at least 12 months—and distinguished the application claims from the prior art based on, *inter alia*, the claimed liquids being stable for at least 12 months. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 19-32, 53-63. Azurity stressed that "the prior art does not provide any expectation that any <u>particular</u> combination would be successful for stable enalapril oral liquid formulations." *Id*. at 23 (emphasis in original). As the Delaware court found, Azurity repeatedly tied alleged unexpected stability of the First Wave Patent claims to "specific concentrations of specific ingredients" of the claims, which were amended to reflect the Example E liquids. *Id*. at 19-22, 28, 58. Azurity made the same types of unexpected results arguments during prosecution of the Second Wave Patents and the '023 patent. Moreton Decl. ¶ 87; *id*. at Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶¶ 33, 63, 124, 158. Thus, Azurity cannot excuse its failure to sufficiently describe stable enalapril liquids sufficient to support the '023 patent claims by pointing to the prior art and arguing that the enalapril liquids generally, or the specific liquids claimed in the '023 patent, were known or would be expected to be stable. *AbbVie*, 759 F.3d at 1301; *Nuvo*, 923 F.3d at 1381, 1384.

b. What Azurity Actually Invented *<u>Versus</u>* What It Has Claimed

i. What Azurity Actually Invented

The common specification generally discloses, *inter alia*, enalapril liquids that can be

stable (defined as having at least 95% enalapril and about 5% w/w or less total impurities) under different conditions for different periods of time. ECF No. 1-1, Compl. Ex. A, '023 patent 18:51-19:48; Moreton Decl. ¶ 67. The specification explains that the enalapril liquids can be stable at refrigerated conditions "for at least 1 month, at least 2 months, at least 3 months, . . . , at least 12 months, . . . , at least 18 months, at least 24 months, ..." ECF No. 1-1, Compl. Ex. A, '023 patent; Moreton Decl. ¶ 67. A POSA would understand this to mean that some of the enalapril liquids disclosed would be stable at refrigerated conditions for at least 1 month, others may be stable for at least 2 months, *etc*.; a POSA would not understand this as suggesting that all of the enalapril liquids disclosed in the specification would be stable for at least 12 months in refrigerated conditions. Moreton Decl. ¶ 67.

Recognizing that the prior art was populated with enalapril liquids that were stable for only a few weeks or months—including the Epaned® Kit, which "was stable for only 60 days once reconstituted" (ECF No. 25, Azurity's Br. at 4)—Azurity realized during prosecution of the First Wave Patents that it would need to limit its claims to only those liquids that were stable for at least 12 months, and to argue that such stability was unexpected, in order to overcome the prior art. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 21-26, 31. However, as the Delaware court found, the only liquids that Azurity described in the specification as being stable for at least 12 months were the Example E liquids, which each contained citric acid/sodium citrate at specific concentrations, and 1 mg/mL of sodium benzoate. *Id*. at 28; ECF No. 1-1, Compl. Ex. A, '023 patent 36:43-37:40; Moreton Decl. ¶¶ 68-69.

Indeed, the common specification contains no other 12-month stability data under any conditions (refrigerated or otherwise) for any other enalapril liquid formulation. Moreton Decl. ¶ 79. And, as Azurity and its expert admitted during the First and Second Wave Suits, some of the

accelerated data presented for other enalapril liquids, such as for the paraben preserved formulations of Example C, suggests that those formulations would likely not be stable at 12 months under refrigerated conditions. Shrestha Decl. Ex. B, D. Del. 18-1962 ECF No. 253, Azurity's PI Mot. Reply Br. at 8; Moreton Decl. ¶¶ 80-82, 85. During trial in the First Wave Suits, Azurity's expert, Dr. Byrn, ***repeatedly characterized the Example C formulations as inoperable***, meaning that, based on the accelerated data presented, those formulations would likely not meet the stability requirements of the claims, an opinion that Bionpharma's expert, Dr. Moreton, agrees with. Moreton Decl. ¶¶ 80-82, 85; *id*. at ¶ 107 (citing to Dr. Byrn's trial testimony). Thus, Azurity limited the claims of its First Wave Patents to cover a very small group of enalapril liquids that require specific concentrations of enalapril, citric acid, sodium citrate, and sodium benzoate, corresponding to the Example E liquids, which were the only enalapril liquids that Azurity actually described in the common specification as being stable for 12 months.

ii. What Azurity Claimed in Second Wave Patents

After Bionpharma filed its ANDA, Azurity began filing applications seeking considerably broader and different claim coverage. During prosecution of the '159 application (which issued into the '482 patent, one of the Second Wave Patents), Azurity sought to claim enalapril liquids with ***any amount*** of citric acid/sodium citrate buffer, and with ***any*** preservative at ***any*** concentration. Moreton Decl. ¶ 73, *id*. at Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶ 15. The Examiner, however, recognized that Azurity was attempting to claim enalapril liquids that were nowhere described in the specification, and issued no less than three separate WD rejections, which required Azurity to narrow its '159 application claims to cover enalapril liquids with a specific range of concentrations of citric acid/sodium citrate buffer, and a specific preservative (either sodium benzoate or a paraben) at a specific concentration (1 mg/mL). Moreton Decl. ¶ 73, *id*. at Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶¶ 16-29, 93-94,

97-102.

But the Examiner also allowed Azurity to claim enalapril liquids with concentrations of citric acid/sodium citrate buffer beyond those of Example E liquids under the mistaken belief that Azurity could supplement the written description of its specification with inventor declarations submitted ***after*** the applications were filed that described additional enalapril liquids as being stable, in violation of fundamental patent law. Moreton Decl. ¶ 73; *Enzo*, 323 F.3d at 969. Partly because Azurity was able to take advantage of the Examiner's failure to understand that a deficient specification cannot be cured by post-application filing declarations, and partly because the Examiner simply failed to appreciate the breadth of the claims that Azurity filed, Azurity was able to secure broad claims in connection with its Second Wave Patents that go well beyond what is described and enabled in the specification. Moreton Decl. ¶ 73.

iii. What Azurity Has Claimed in the '023 Patent

As with the Second Wave Patents, Azurity has leveraged the PTO Examiner's mistaken belief that a deficient specification can be supplemented with inventor declarations to secure patent claims that are broader in scope than the claims of the First Wave Patents (which claim what Azurity actually invented)[5] and that cover enalapril liquids nowhere described in the common specification as being stable for at least 12 months under refrigerated conditions. To begin with, although the claims of the '023 patent do not expressly require a buffer, they may nevertheless include a buffer or buffers, and at varying concentrations.[6] Moreton Decl. ¶ 75. The '023 patent

[5] While the claims of the '023 patent are broader than the claims of the First Wave Patents, they are commensurate in scope with the claims of the Second Wave Patents (which themselves are broader in scope than the claims of the First Wave Patents). Moreton Decl. ¶¶ 71, 75.

[6] Azurity has listed the '023 patent in the FDA's Orange Book for Epaned®, which means that Azurity believes that the claims of the '023 patent cover Epaned®, which contains a citric acid/sodium citrate buffer. *See* 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.53(b); ECF No. 9-23, 7/13/21 Shrestha Decl. Ex. W, Orange Book Entry for Epaned®; ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 6. Thus, the '023 patent claims cover enalapril liquids with buffers.

claims also include within their scope enalapril liquids with sweeteners and flavoring agents, which are not restricted by concentration. The common specification identifies at least 38 different buffering agents, at least 47 different flavoring agents, and approximately 38 different sweeteners that may be used in the claimed liquids. ECF No. 1-1, Compl. Ex. A, '023 patent 8:45-9:16, 13:35-57, 17:61-18:18; Moreton Decl. ¶¶ 75-76. Furthermore, 18 of the 20 claims of the '023 patent (claims 1-3 and 6-20), have no restriction on pH, an incredibly important factor for stability of enalapril in liquid formulations, which the Examiner likely overlooked. Moreton Decl. ¶¶ 100-102; *id*. at Ex. G, 18-1962 ECF No. 235, 3/31/21 Byrn Decl. ¶ 18; ECF No. 25-6, Buckton Decl. ¶ 23. And because of the "consisting essentially of" transitional phraseology used in the claims of the '023 patent, and the "comprising" language used in connection with the preservative limitations, excipients beyond those expressly recited may be included as long as they do not materially affect the basic and novel characteristics of the claimed liquids. *HZNP Meds. LLC v. Actavis Labs. UT, Inc*., 940 F.3d 680, 692–93 (Fed. Cir. 2019); Moreton Decl. ¶ 37. As Dr. Moreton explains:

> All of these different combinations, at different concentrations, and different pHs, and with different concentrations of enalapril that are permitted ("about 0.6 to about 1.2 mg/ml"), leads to an incredibly large number of enalapril liquids that can meet the formulation elements of the '023 patent claims. I conservatively put the number at tens of thousands of potential liquids, but it is more likely hundreds of thousands of enalapril liquids that meet the formulation elements of the claims.

Id. at ¶ 76.

c. The POSA Would *Not* Believe that Azurity Possessed Hundreds of Thousands of Stable Liquids

The formulations elements the '023 patent claims go well beyond the Example E liquids (the ***only*** liquids described in the common specification as being stable for at least 12 months), and a POSA would simply not believe that Azurity possessed tens (let alone hundreds) of thousands of enalapril liquids that meet the claimed stability requirements because numerous aspects of the

'023 patent claims have no support in the common specification.

i. There Is *No* Description of Stable Enalapril Liquids *without a Buffer*

For instance, in contrast to the claims of the First and Second Wave Patents, the claims of the '023 patent cover stable enalapril liquids that do not contain a buffer. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; ECF No. 25, Azurity's Br. at 17. Azurity describes this as a "dramatic[] change[in] the scope of the claims of the '023 Patent from those previously asserted in the [First Wave Suits]." ECF No. 25, Azurity's Br. at 17. However, while Azurity is correct that the common specification broadly discloses that "[i]n some embodiments, the oral liquid formulation comprises a buffer," ECF No. 25, Azurity's Br. at 16-17 (citing ECF No. 1-1, Compl. Ex. A, '023 patent at 13:58-59), ***all*** of the enalapril liquids described in the common specification include a separate buffer component—and a specific one at that: a citric acid and sodium citrate buffer. ECF No. 1-1, Compl. Ex. A, '023 patent at Examples A-G; Moreton Decl. ¶ 89. And, as the Delaware court found after trial in the First Wave Suits, the only enalapril liquids described as being stable for at least 12 months—the Example E liquids—all contain a citric acid and sodium citrate buffer and specific concentrations. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 28; Moreton Decl. ¶ 92 ("[E]very example of an enalapril liquid in the common specification contains enalapril maleate and a separate, independent 'buffering agent.'").

There is simply no description in the common specification of an enalapril liquid that does not contain a separate buffer component, let alone one that is stable for at least 12 months under refrigerated conditions. Moreton Decl. ¶¶ 88-93. As Azurity admits, this is a "dramatic[] change[]" (ECF No. 25, Azurity's Br. at 17), because, as the Delaware court found, the purpose of a buffer in the claimed liquids is to maintain the formulation pH. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 37-38. And as Azurity's expert in the instant suit, Dr. Buckton, admits,

"modulation of pH provides a lowered impurity profile." ECF No. 25-6, Buckton Decl. ¶ 23. Furthermore, as the Delaware court also found, Azurity submitted a Citizen Petition to FDA in 2017 arguing that a citric acid and sodium citrate buffer was absolutely critical to the stability of enalapril liquids both during storage and in the stomach after ingestion, such that "[a]ny change in the amount of citric acid or sodium citrate [buffer], ***removal of one or more [of] these [buffers]***, or replacement with different buffering components, could materially affect" the stability and dosing of the enalapril. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 42-43, 66-67; Shrestha Decl. Ex. D, 4/3/17 Azurity Citizen Petition at 1, 8. In its Post-Trial Answering Brief in the First Wave Suits, Azurity argued that "enalapril must remain within a very narrow pH range to prevent degradation [and thus maintain stability]," and that the only way to do that is by including a buffer. Shrestha Decl. Ex. D, D. Del. 18-1962 ECF No. 218, Azurity's Post-Trial Answering Br. at 3.

Azurity and its experts have made repeated representations regarding the importance of a buffer to modulate pH and stabilize enalapril, yet Azurity provides no example in the common specification of any enalapril liquid without a separate buffer component, let alone one that would be stable for at least 12 months under refrigerated conditions. For these reasons, a POSA would understand that the specification contains no WD of stable enalapril liquids without a buffer.

ii. Many Other Aspects of the Claims Are Not Described

Several other aspects of the '023 patent claims are nowhere described in the common specification, let alone as resulting in liquids that are stable for at least 12 months under refrigerated conditions. Some examples include:

> **Paraben Preserved Formulations**: The formulation elements of claims 1-16 and 19 include within their scope enalapril liquids where the only preservative is a paraben or mixture of parabens. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; Moreton Decl. ¶¶ 80, 107. There is no description in the specification of a paraben preserved enalapril liquid that is stable for at least 12 months. *Id*. Quite the opposite: as Dr. Moreton explains, and as Azurity and its expert conceded in the First Wave Suits, the accelerated data provided for the paraben preserved enalapril liquids of Example C would convince a POSA

that those liquids would likely ***not be stable*** for 12 months at refrigerated conditions. Shrestha Decl. Ex. B, D. Del. 18-1962 ECF No. 253, Azurity's PI Mot. Reply Br. at 8; Moreton Decl. ¶¶ 80-82, 85, 107. Those inoperable Example C formulations fall within the literal scope of the formulation elements of many of the '023 patent claims. Moreton Decl. ¶ 80; ECF No. 1-1, Compl. Ex. A, '023 patent at Example C and claims.

No pH Restriction: Claims 1-3 and 6-20 of the '023 patent have no restriction on pH. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; Moreton Decl. ¶ 102. The only liquids described in the specification as being stable for at least 12 months—the Example E liquids—had pHs of 3.3-3.4. ECF No. 1-1, Compl. Ex. A, '023 patent at Example E; Moreton Decl. ¶ 100. As Azurity and its experts have admitted, enalapril was known to be stable only within a very narrow pH range (3-3.5). Shrestha Decl. Ex. C, D. Del. 18-1962 ECF No. 218, Azurity's Post-Trial Answering Br. at 3; Moreton Decl. Ex. G, D. Del. 18-1962 ECF No. 235, 3/31/21 Byrn Decl. ¶ 18 ("pH is related to stability, and pH changes will cause [enalapril] to degrade."); ECF No. 25-6, Buckton Decl. ¶ 23. The specification teaches that enalapril degradation into enalaprilat and enalapril diketopiperazine increases at pHs above 3.5 and below 4, respectively, and a POSA would know that the optimal pH for enalapril stability is around 3. Moreton Decl. ¶¶ 100-102. There is no description of an enalapril liquid stable for at least 12 months at a pH beyond 3.3-3.4, nor would a POSA believe Azurity possessed such liquids at the time it filed for the '023 patent. *Id*.

Buffers Beyond Citric Acid/Sodium Citrate: As explained above and in Dr. Moreton's Declaration, the formulation elements of the '023 patent claims cover enalapril liquids that include buffers (even though they are not expressly required), and the specification lists at least 38 different kinds of buffering agents that may be used. Moreton Decl. ¶ 94. As the Delaware court found, Azurity argued in a 2017 Citizen Petition to FDA that a citric acid/sodium citrate buffer was critical to stability of enalapril in a liquid. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 42-43, 66-67; Shrestha Decl. Ex. D, April 3, 2017 Azurity Citizen Petition at 1, 8. The only liquids in the specification described as stable for at least 12 months (Example E liquids) use a citric acid/sodium citrate buffer. *Id*. There is no description of an enalapril liquid stable for at least 12 months that uses any other kind of buffer. *Id*.

Buffer Concentration beyond 5-20 mM: The molar concentration of citric acid/sodium citrate buffer in the Example E liquids is between 5-20 mM; however, even though the '023 patent claims include liquids with buffers, there is no restriction on buffer concentration. Moreton Decl. ¶¶ 110-111. As the Delaware court found, Azurity argued in a 2017 Citizen Petition to FDA that buffer concentration was critical to stability of enalapril in a liquid. ECF No. 9-7, 7/13/21 Shrestha Decl. Ex. G, Op. at 42-43, 66-67; Shrestha Decl. Ex. E, 4/3/2017 Azurity Citizen Petition at 1, 8. There is no description of an enalapril liquid with a buffer concentration beyond 5-20 mM that is stable for at least 12 months. Moreton Decl. ¶ 110-111.

Sugars/Sugar Alcohols: The specification expressly warns that many sugars and sugar alcohols used as sweeteners can react with paraben preservatives to create additional degradants, but the '023 patent claims permit or require the inclusion of sugar/sugar alcohol sweeteners and paraben preservatives. ECF No. 1-1, Compl. Ex. A, '023 patent 13:18-31;

id. at claims; Moreton Decl. ¶¶ 112-113. There is no WD of a paraben preserved enalapril liquid that includes a sugar/sugar alcohol and is stable for at least 12 months. Moreton Decl. ¶¶ 112-113.

Sodium Benzoate Concentration Beyond "about 1 mg/ml": The '023 patent claims either require (*e.g.*, claims 17-18 and 20) or permit (*e.g.*, claims 1-12, 14-16, 19) the inclusion of sodium benzoate as a preservative. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; Moreton Decl. ¶ 132. There is no description in the common specification of an enalapril liquid with a sodium benzoate concentration beyond "about 1 mg/ml" that is stable for at least 12 months, yet the '023 patent claims permit greater or lesser amounts of sodium benzoate. *Id*.

Stability Longer than 12 Months: The '023 patent claims 2 and 3 require stability for at least 18 months and at least 24 months, respectively. ECF No. 1-1, Compl. Ex. A, '023 patent at claims; Moreton Decl. ¶ 103. However, the common specification describes no enalapril liquid that is stable longer than 62 weeks (a little over a year). Moreton Decl. ¶¶ 103-106.

The above described enalapril liquids, which fall within the scope of the '023 patent claims, are nowhere described in the common specification, and a POSA would not believe that Azurity possessed such formulations at the time it filed for the '023 patent.

d. Case Law Supports a Finding of Invalidity for Lack of WD

The Federal Circuit's decisions in *Idenix Pharmaceuticals LLC v. Gliead Sciences, Inc.*, 941 F.3d 1149 (Fed. Cir. 2019) and *Nuvo* strongly support a finding of lack of WD for the '023 patent claims. In *Idenix*, the claims were directed to a method of treating Hepatitis C virus ("HCV") by administering a "β-D-2'-methyl-ribofuranosyl nucleoside" with a methyl group in the 2' up position, and any substituent in the 2' down position. *Idenix*, 941 F.3d at 1154-55. The accused infringer's product used a nucleoside with a fluorine group in the 2' down position, but such a compound was nowhere described in the specification, let alone as effective in treating HCV, which led the Federal Circuit to find the claims invalid for lack of WD. *Id*. at 1163-65.

The claims in *Nuvo* were directed to a pharmaceutical composition with a NSAID (non-steroidal anti-inflammatory drug) core surrounded by a layer of an acid inhibitor, such as a proton-pump inhibitor ("PPI"), effective to raise gastric pH to 3.5, where at least some of the PPI is

uncoated. *Nuvo*, 923 F.3d at 1372-73. The brand insisted as part of its response to the generics' obviousness case that a POSA "would not have expected uncoated PPIs to be effective," but there was nothing in the specification supporting the efficacy of uncoated PPI of the claims to raise gastric pH. *Id*. at 1377. The *Nuvo* court found the claims invalid for lack of WD for failing to demonstrate that uncoated PPI would be effective in raising gastric pH to 3.5. *Id*. at 1381-84.

Pernix Ireland Pain DAC v. Alvogen Malta Operations, Ltd., 323 F. Supp. 3d 566 (D. Del. 2018) is very similar to the facts of the instant case and supports Bionpharma's lack of WD defense. There, Federal Circuit Judge Bryson, sitting in the District of Delaware by designation, found that claims directed to methods of treating pain in a patient having mild/moderate hepatic impairment that covered the use of nearly any hydrocodone extended release formulation to achieve certain functional requirements were not adequately described when the specification only described one formulation that would meet the claims' functional limitations. *Id*. at 617-630. *Idenix, Nuvo*, and *Pernix* strongly support a lack of WD finding.

Azurity's reliance on the *Alcon Research Ltd. v. Barr Laboratories, Inc.*, 745 F.3d 1180 (Fed. Cir. 2014) is misplaced. ECF No. 25, Azurity's Br. at 17. In *Alcon*, the claims were directed a method of enhancing the chemical stability of an aqueous composition of a known drug by adding "a chemically stabilizing amount of a polyethoxylated castor oil . . . to the composition." *Alcon*, 745 F.3d at 1184. The Federal Circuit there rejected a WD challenge because the specification "referenced the unexpected nature of the discovery, gave exemplary formulations, and disclosed data showing stability testing using the claimed invention." *Nuvo*, 923 F.3d at 1382 (discussing and distinguishing *Alcon*); *Alcon*, 745 F.3d at 1191. By contrast, here, the common specification only describes 6 liquids—the Example E liquids, which are all of similar composition (each containing 1 mg/mL of enalapril maleate, specific concentrations of citric acid/sodium citrate

buffer, and 1 mg/mL of sodium benzoate, at a pH of 3.3-3.4)—as being stable for at least 12 months under refrigerated conditions. However, as explained above, the claims of the '023 patent are much broader than the Example E liquids, and encompass tens (if not hundreds) of thousands of enalapril liquids that do not even resemble the Example E liquids. *Pernix* is instructive on this point. There, the specification described one formulation that would meet the functional limitations of the claims—this was not enough to support the broad genus claims at issue there. *Pernix*, 323 F. Supp. 3d at 628 ("Therein lies the written description problem: the claims are far broader than the disclosure."). What Azurity has "claimed [in the '023 patent does] not correspond to what [is] described," requiring a finding of invalidity due to lack of WD. *Id*.

2. The '023 Patent Claims Are Not Enabled

As explained above, the formulation elements of the claims of the '023 patent cover tens (likely hundreds) of thousands of enalapril liquids, and include within their scope the Example C liquids, which Azurity and its expert in the First and Second Wave Suits admitted are inoperable (i.e., would not be expected to be stable for at least 12 months under refrigerated conditions). Moreton Decl. ¶¶ 75-76, 80-82, 114-116. The formulation elements of the '023 patent claims also cover enalapril liquids that (1) include paraben preservatives and sugars/sugar alcohols (as sweeteners), and (2) that have a pH outside of 3-3.5, which a POSA would believe would not meet the stability elements of the claims (and would therefore be inoperable). *Id*. ¶ ¶ 83, 114. "A claim is not enabled when, at the effective filing date of the patent, [a POSA] could not practice their full scope without undue experimentation." *Idenix*, 941 F.3d at 1154 (internal quotations omitted). Applying the *Wands* Factors shows that determining which liquids falling within the scope of the '023 patent claims are operable would not only require undue experimentation, it would be scientifically inconceivable. Moreton Decl. ¶¶ 117-128.

The quantity of experimentation required would be enormous: a POSA would have to

prepare tens (likely hundreds) of thousands of enalapril liquids and subject all of them to stability testing under refrigerated conditions for at least 12 months, and up to 24 months, and then analyze the results. *Id*. ¶ 118. As Dr. Moreton explains, this experimentation is not routine; it is essentially impossible. *Id*. The specification contains only six working examples (the Example E liquids), which are very similar in composition, and represent a very small sliver of the broad genus of liquids claimed in the '023 patent. *Id*. ¶¶ 120-122. "Where, as here, working examples are present but are very narrow, despite the wide breadth of the claims at issue, this factor weighs against enablement." *Idenix*, 941 F.3d at 1161 (internal quotations omitted).

With respect to the amount of guidance provided, while the specification warns that enalapril degradation increases at certain pHs, and that paraben preserved formulations with sugars/sugar alcohols should be avoided, the POSA would not find those teachings helpful because most of the '023 patent claims are not restricted by pH (or permit pH up to 4), and expressly permit paraben preserved formulations with sweeteners. Moreton Decl. ¶ 123. Regarding the nature and predictability of the field, as explained above, enalapril liquid stability is unpredictable (as Azurity and its expert repeatedly represented (*see* Argument § II.B.1.a, *supra*)), and the presumption is that enalapril liquids are not stable long-term. *Id*. ¶¶ 124-125. Azurity admits that the prior art provides no guidance. *Id*. All the *Wands* Factors support non-enablement, and *Idenix* is directly on point. *See also Wyeth and Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir.2013) (affirming non-enablement under similar facts).

Finally, Azurity's argument that the claims are enabled because "[t]he specification instructs that the amount of impurities is dependent on the pH" ignores the fact that 18 of 20 of the '023 patent claims ***contain no restriction on pH whatsoever***, and the two that do (claims 4 and 5) allow a pH up to 4, well beyond the range of 3-3.5 that the specification teaches is optimal.

Moreton Decl. ¶¶ 100-102. And, the '023 patent claims ***do not*** require a buffer—which is what maintains formulation pH. *Id*. ¶ 90. Enablement "considers the scope of the claim as written, not just the subset of the claim that a POSA might practice." *Idenix*, 941 F.3d at 1162. Thus, the sheer breadth of the claims supports non-enablement. *Id*.

3. If Adequately Supported, the Asserted Claims Are Obvious

Upon reconstitution, Azurity's predecessor product, Epaned® Kit, was a 1 mg/ml enalapril maleate oral liquid that contained a citric acid/sodium citrate buffer; methylparaben and propylparaben as preservatives; a flavoring agent; purified water; and glycerin, sorbitol, and sodium saccharin as sweeteners. Moreton Decl. ¶ 129; *id*. at Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶¶ 187, 264; ECF No. 1-1, Compl. Ex. A, '023 patent at 8:44-60 (identifying glycerin, sorbitol and sodium saccharin as sweeteners); Shrestha Decl. Ex. E, Epaned® Kit PI at DTX2064.11. As Bionpharma's expert, Dr. Moreton, explains, a POSA would have been motivated to reformulate the Kit to a ready-to-use ("RTU") formulation to increase patient compliance by making administration easier (important in the pediatric population), and to increase efficiency from a supply chain and cost perspective, as reformulation to an RTU would eliminate the need for multiple bottles and the use of a proprietary diluent. Moreton Decl. Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶ 192.

In reformulating the Kit, the POSA would: (1) target a pH of around 3, because that was known to be the pH of maximum stability for enalapril in solution, (2) remove the solid excipients, such as mannitol and colloidal silicon dioxide ("CSD"); and (3) remove potassium sorbate, which was known to destabilize liquid formulations in plastic containers. *Id*. ¶¶ 193-200, 262-263. The excipients remaining after removal of mannitol/CSD/potassium sorbate are either permitted by the claims or would be removed if found through routine experimentation to adversely impact stability. *Id*. ¶ 264.

With respect to the stability limitations, the '747 patent, which covered the Kit, teaches the degradation of enalapril and provides the "at least 95% enalapril/less than about 5% impurities" benchmark recited in the claims, and discloses that enalapril stability is maximized in refrigerated conditions and can be up to 36 months. *Id*. ¶ 201. From the FDA Stability Guidance, the POSA would have targeted at least 12 months, but more preferably 24 months, of stability for a product stored in refrigerated conditions, and would have reasonably expected to achieve this through routine experimentation. *Id*.

Moreover, in response to Bionpharma's WD and enablement defenses, Azurity appears to argue that enalapril liquid formulations covered by the formulation elements of the Asserted Claims are all ***inherently*** stable (ECF No. 25, Azurity's Br. at 15-17); otherwise, Azurity has the very non-enablement problem Bionpharma pleads above, with numerous liquids falling within the scope of the formulation elements but not meeting the stability requirements. If true, then Bionpharma does not need to establish that the stability limitations were obvious. *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012) (obvious formulation does not become non-obvious by claiming inherent property). This is so because the formulation elements of the Asserted Claims read on an obvious formulation. For instance, as explained above, a POSA reformulating the Kit into a RTU formulation would wind up with a liquid that contained 1 mg/ml of enalapril maleate; approximately 1 mg/ml of methylparaben and propylparaben as a preservative (combined); sodium citrate and citric acid as a buffer (which would not be excluded from the '023 patent claims), a flavoring agent, water, and a sweetener (glycerin/sorbitol/sodium saccharin). Moreton Decl. ¶ 129; *id*. at Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶¶ 187-204, 262-267. The formulation elements of claim 1 would literally read on that obvious formulation, and Azurity cannot avoid obviousness by claiming an inherent property.

With respect to reasonable expectation of success, as Dr. Moreton explains, "a POSA could set out to prepare an enalapril liquid[] as . . . outlined above, and would reasonably expect, using routine optimization, that the formulation could be developed to be stable for at least 12 months at refrigerated conditions." Moreton Decl. Ex. C, D. Del. 18-1962 ECF No. 247, 4/19/21 Moreton Decl. ¶ 203. Finally, as Dr. Moreton explains, the Mosher Declaration submitted during prosecution of the '023 patent does not establish unexpected results because Dr. Mosher came forward with no data showing that the formulations exemplified therein would be stable for 12 months under refrigerated conditions, and Dr. Mosher's extrapolation of the 12-week data contained in the Mosher Declaration is scientifically improper. Moreton Decl. ¶ 131.

III. AZURITY HAS FAILED TO ESTABLISH IRREPARABLE HARM

A. Azurity's Delays and Lack of Diligence Undermine Harm Allegations

"[D]elay in seeking a remedy is an important factor bearing on the need for a [PI]." *High Tech Med. v. New Image*, 49 F.3d 1551, 1557 (Fed. Cir. 1995). "Absent a good explanation," a delay in seeking relief "militates against the issuance of a [PI]." *Id*. Azurity's repeated delays surrounding the '023 patent counsel against an irreparable harm finding.

First, Azurity began filing for its First Wave Patents back in 2016 (ECF No. 9-3, 7/13/21 Shrestha Decl. Ex. C, '008 patent at cover), but waited to file for the '023 patent until January 15, 2021 (ECF No. 1-1, Compl. Ex. A, '023 patent at cover), almost 2.5 years ***after*** Bionpharma filed its ANDA (Aug. 31, 2018). Azurity could have, and should have, filed for the '023 patent earlier. Its failure to do so represents a strategic, improper, last-ditch attempt by Azurity to stave off generic competition after Bionpharma prevailed against Azurity in three prior suits involving seven patents in the same family as the '023 patent. Second, once the '023 patent issued (June 22, 2021), Azurity still delayed seeking emergency relief. While Azurity filed suit that same day, it waited for almost two months after it filed suit, and ***nine days after Bionpharma's ANDA was***

given final approval, to finally seek emergency relief. Background § III, *supra*. Azurity knew that the 30-month stay of FDA approval of Bionpharma's ANDA had expired on April 30, 2021, and FDA was thereafter free to finally approve Bionpharma's ANDA, leading to an imminent launch. Azurity's delays in filing for the '023 patent and in seeking emergency relief counsel against a finding of irreparable harm.

B. Azurity Has Failed to Show Irreparable Harm to Itself

[redacted] McSorley Decl. ¶ 17; ECF No. 25, Azurity's Br. at 1 n.1; ECF No. 25-8, Patel Decl. ¶ 1. Because Azurity has failed to show that it [redacted] will actually suffer irreparable harm, an injunction cannot issue. *Voda v. Cordis Corp.*, 536 F.3d 1311, 1329 (Fed. Cir. 2008).

C. Any Damages Would Be Quantifiable

Azurity's assertion that it will suffer irreparable harm from decreased revenue and market share upon launch of Bionpharma's ANDA product (ECF No. 25, Azurity's Br. at 18-20) is simply false. Loss of sales and market share, even if difficult to calculate, is not enough to establish irreparable harm. *Novartis Corp. v. Teva Pharm. USA, Inc.*, Civ. No. 04-4473 (HAA)(ES), 2007 WL 1695689, at *26-*27 (D.N.J. Jun. 11, 2007); *Nutrition 21 v. United States*, 930 F.2d 867, 871 (Fed. Cir. 1991). Here, as Bionpharma's expert, Mr. McSorley, explains, Azurity has come forward with [redacted] McSorley Decl. ¶¶ 20-24. As Mr. McSorley explains,

Azurity's expert (Dr. Stec) "fails to provide any factual, credible rationale as to [redacted] do not constitute the type of reliable economic evidence that provides a reasonable basis for the quantification of potential loses in this case. *Id.* ¶ 27; *Graceway Pharm., LLC v. Perrigo Co.*, 722 F. Supp. 2d 566, 577 (D.N.J. 2010); *Eli Lilly & Co. v. Am. Cyanamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996). Mr. McSorley also explains that, contrary to Azurity's and Dr. Stec's assertion (ECF No. 25, Azurity's Br. at 19 n.12), prior precedent from Apotex Inc.'s at-risk launch of generic Plavix® illustrates the quantifiable nature of Azurity's alleged losses. *Id.* ¶¶ 29-31. Plavix®, another oral drug used to treat heart disease, rebounded entirely after the generic (Apotex) was removed from the market a few weeks after an at-risk launch in August 2006—even though Apotex had shipped quantities that remained in distributors' inventories until 2007—and the brand sustained no long-term adverse impact. McSorley Decl. ¶¶ 29-31.

Moreover, as explained above, there is no evidence that Azurity [redacted] *Poly-America, L.P. v. GSE Lining Tech., Inc.*, 383 F.3d 1303, 1311 (Fed. Cir. 2004). Thus, if Azurity succeeds in proving infringement, [redacted] which, as Mr. McSorley explains, is easily quantifiable, including because of the existence of acceptable, non-infringing alternatives. McSorley Decl. ¶¶ 16-17, 32-40.

Further, Azurity's claim of [redacted] is belied by [redacted]. *Id.* ¶ 25; ECF No. 25-8, Patel Decl. ¶ 16. Moreover, Azurity's claims of [redacted] are speculative but can be quantified. McSorley Decl. ¶¶ 20-28; *Novartis*, 2007 WL 1695689, at *27 (rejecting claim that price erosion was unquantifiable). Azurity's additional claims of [redacted]

[redacted] (ECF No. 25, Azurity's Br. at 21-22) are also speculative and undermined by the fact that the importance of Epaned® to Azurity is declining, particularly with its recent acquisition of Arbor Pharmaceuticals: [redacted] and would be expected to decrease with the Arbor aquisition. McSorley Decl. ¶¶ 18-19, 41-54. Further, lost research opportunities have been rejected by the Federal Circuit as grounds for irreparable harm. *Eli Lilly*, 82 F.3d at 1578.

IV. THE BALANCE OF HARDSHIPS AND PUBLIC POLICY SUPPORT DENIAL

Azurity does not seek to preserve the status quo; rather, it seeks to alter it by requesting that Bionpharma be ***removed from the market*** (Bionpharma has already launched) after Azurity has enjoyed a full 30-month stay of approval of Bionpharma's ANDA, with a patent that Azurity could have filed for much earlier. Bionpharma has made a significant investment in its design-around product, and has waited 30 months so that the parties could secure certainty over Azurity's First Wave Patents. Any further restriction on launch of Bionpharma's ANDA is simply prejudicial to Bionpharma, as Bionpharma is currently enjoying its 180-day exclusivity period. McSorley Decl. ¶¶ 55-58. The "public interest [favors] receiving generic competition to brand-name drugs as soon as is possible." *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1, 203 (D.D.C. 1997); McSorley Decl. ¶¶ 59-63. The desperate public need for generic competition for Epaned® has been prominently featured in the news media, including the Washington Post, which noted that Epaned® falls into a category of drugs where the brand (Azurity) creates a liquid formulation of an old drug and charges exorbitant prices for the reformulated drug, posing an incredible financial burden to families. Shrestha Decl. Ex. F, Shefali Luthra, *The dilemma of kid-friendly pharmaceuticals: Safety comes at a steep price*, WASHINGTON POST (Apr. 21, 2017).

V. AZURITY MUST POST A BOND

If the Court is inclined to grant the extraordinary relief Azurity seeks, Bionpharma respectfully requests that Azurity be required to post a bond to secure Bionpharma's rights in an amount identified in paragraphs 64-68 of the McSorley Declaration. FED. R. CIV. P. 65(c). *Frank's GMC Truck Center, Inc. v. General Motors Corp.*, 847 F.2d 100 (3d Cir. 1988) ("[A]bsent circumstances where there is no risk of monetary loss to defendant, the failure of a district court to require a successful applicant to post a bond constitutes reversible error.").

CONCLUSION

Bionpharma respectfully requests that Azurity's Motion be denied.

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Respectfully submitted,

/s/ Thomas R. Curtin

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